REMARKS

Claims 1-26 are pending in the subject application. By this Amendment, applicants have canceled claims 17, 25 and 26 and have amended claims 1, 3, 7, 9, 15 and 16. Applicants maintain that the changes to claims 1, 3, 7, 9, 15 and 16 raise no issue of new matter. Accordingly, claims 1-16 and 18-24 are pending and under examination.

In view of the arguments below, applicants maintain that the Examiner's rejections have been overcome, and respectfully request that they be withdrawn.

Rejection Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 16-18, 25 and 26 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. Specifically, the Examiner alleges that the phrases "substance which inactivates mRNA" in claim 16 and 17, "linked to a regulatory subunit" in claim 18 and "adapted for passage through a plasma cell membrane" are vague and unclear.

In response, but without conceding the correctness of the Examiner's rejection, applicants note that claims 17, 25 and 26 have been canceled and claim 16 has been amended to delete the phrase "substance which inactivates mRNA." In regards to claim

18, applicants respectfully traverse the Examiner's rejection. Claim 18 reads, in relevant part, "linked to a regulatory *element*", not "linked to a regulatory subunit" as the Examiner alleges. Applicants contend that the phrase "regulatory element" is clearly defined in the specification *inter alia* at page 21, lines 18-23.

In view of these remarks, applicants maintain that amended claim 16 and claim 18 satisfy the requirements of 35 U.S.C. §112, second paragraph, and request that the rejection be withdrawn.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1-26 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that the genus of nucleic acids encoding DNA-dependent protein kinase catalytic subunit, Ku70 or Ku80 is highly varied as structural attributes which define the members of the genus are missing from the disclosure.

Applicants note that claims 17, 25 and 26 have been canceled rendering the rejection thereof moot. In response to the rejection of the remaining claims, applicants respectfully traverse.

The test for written description under 35 U.S.C. §112, first paragraph, is whether the disclosure describes the claimed invention in sufficient detail so that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. According to M.P.E.P. §2163(I)(A), when evaluating whether support in the specification for the original claims is sufficient, "[t]here is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). The initial burden is therefore on the Examiner to present evidence of the lack of written description. Applicant maintains that the claimed invention satisfies the test for adequate written description, and that the Examiner has not set forth sufficient grounds for concluding otherwise.

The subject invention provides antisense oligonucleotides which specifically hybridize to nucleic acids encoding DNA-dependent protein kinase subunits and methods for using such antisense oligonucleotides. As detailed in the specification *inter alia* at page 1, line 31 to page 2, line 1, DNA-dependent protein kinase catalytic subunit, Ku70 and Ku80 are subunits of the DNA-dependent protein kinase (DNA-PK), a protein complex well documented in the art. The antisense oligonucleotides in the claimed genus are limited to specifically hybridizing to one of these three subunits whose sequences are also well known in the art. One skilled in the pertinent art would recognize the scope to which the genus is limited, i.e. antisense oligonucleotides

of DNA-PK subunits. In view of these remarks, applicants maintain that claims 1-16 and 18-24 are adequately supported by the disclosure and satisfy the written description requirements of 35 U.S.C. §112, first paragraph.

Rejection Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1-14 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Examiner alleges that, although enabled for compositions and methods comprising *in vitro* administration of the antisense oligonucleotides, the specification is not enabled for *in vivo* administration to a subject.

In response, applicants respectfully traverse the Examiner's rejection.

The test for enablement is whether one skilled in the art could, at the time of the invention, make and use the claimed invention based on the disclosure and the information known in the art without undue experimentation. Applicants maintain that the claimed invention satisfies the test for enablement, and that the Examiner has not set forth sufficient grounds for concluding otherwise.

As stated above, the subject invention provides antisense oligonucleotides which specifically hybridize to nucleic acids encoding DNA-dependent protein kinase subunits and methods for using such antisense oligonucleotides. This invention is a result of applicants' discovery of the function of the DNA-PK subunits. As detailed in the specification *inter alia* at page 55, line 36, to page 56, line 6, and at page 56, lines 24-27, applicants discovered that cells lacking DNA-PK subunits have increased sensitivity to radiation-induced apoptosis.

In support of the rejection, the Examiner alleges that the specification does not reasonably enable the claimed methods *in vivo*. Specifically the Examiner alleges that one skilled in the art would not be able to use the invention based on the examples provided in the specification.

Applicants disagree with the Examiner's position. Applicants direct the Examiner's attention to the specification *inter alia* at page 51, lines 6-24. These experiments show that cells deficient in DNA-PK subunits have an increased sensitivity to radiation. Further, Figure 9A shows the radiosensitivity of Ku70-deficient fibroblasts, i.e. *in vitro* and Ku70-deficient mice, i.e. *in vivo*. In both instances, a decrease in radiation tolerance was demonstrated. Applicants maintain that one skilled in the art would recognize the significance of this finding both *in vitro* where cell cultures may be manipulated and *in vivo* to increase the effectiveness of the radiation therapy. Applicants maintain that the target administration of drug

products to tumors in order to aid in radiation therapy is well known in the relevant art. The Examiner has not set forth sufficient evidence to show otherwise. Accordingly, applicants maintain that the specification coupled with the information known in the art clearly enables one skilled in the art to practice the claimed invention.

In view of these remarks, applicants maintain that claims 1-14 satisfy the enablement requirements of 35 U.S.C. §112, first paragraph.

Rejections under 35 U.S.C. §102(e)

The Examiner rejected claim 15 under 35 U.S.C. §102(e) as allegedly anticipated by Hasty et al. (U.S. Patent No. 5,955,644).

Under 35 U.S.C. §102(e), a person shall be entitled to a patent unless the invention was described in a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent. According to MPEP §2131.01, "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

In response, applicants note that Hasty et al. does not teach

each and every element of amended claim 15. Claim 15 provides for an antisense oligonucleotide that specifically hybridizes to a nucleic acid encoding either a DNA-PK catalytic subunit or a Ku70 subunit. Applicants maintain that Hasty et al. teach an antisense molecule that hybridizes to Xrcc5, i.e. Ku86 or Ku80. Hasty et al. does not disclose antisense oligonucleotides hybridizing to either a DNA-PK catalytic subunit or a Ku70. Accordingly, applicants maintain that amended claim 15 is not anticipated by Hasty et al.

The Examiner further rejected claims 15, 23, 25 and 26 under 35 U.S.C. §102(e) as allegedly anticipated by Housman et al. (U.S. Patent No. 6,200,754).

In response, applicants respectfully traverse the Examiner's rejection.

Housman et al. teach antisense oligonucleotides that specifically hybridize to target variance sequences on at least one, but not all, allelic forms of a gene that encodes a gene product essential to cell growth or cell viability. These variance sequences discriminate between allelic forms. Hence, the antisense oligonucleotide cannot hybridize to all allelic forms of the target gene, allowing normal gene product to be produced. In contrast, applicants' invention necessitates that no gene product be produced, i.e. that the expression of the DNA-PK subunit be prevented. The invention therefore provides for an antisense oligonucleotide which can hybridize to all

allelic forms of the DNA-PK subunits. Housman et al. fail to teach the essential inhibition of the gene, so that the lack of double-stranded break repair increases the cell's sensitivity to radiation. Accordingly, applicants maintain that claims 15 and 23 are not anticipated by Housman et al. The rejection of claims 25 and 26 is moot in view of their cancellation.

In view of these remarks, applicants maintain that claims 15 and 23 satisfy the requirements of 35 U.S.C. §102(e), and request that the rejections be withdrawn.

Rejection Under 35 U.S.C. §103(a)

The Examiner rejected claims 15 and 18-24 under 35 U.S.C. §103(a) as allegedly unpatentable over Housman et al. in view of Chiorini et al.

In response to the Examiner's rejection, applicants respectfully traverse, and maintain that the Examiner has failed to establish a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, the Examiner must demonstrate three criteria with respect to each claim. First, the cited references, when combined, teach or suggest every element of the claim. Second, one of ordinary skill would have been motivated to combine the teachings of the cited references at the time of the invention. And third, there would have been a reasonable expectation that the claimed invention

would succeed.

In light of these requirements, applicants maintain that the cited references fail to support a *prima facie* case of obviousness for claims 15 and 18-24.

As stated above, the subject invention provides antisense oligonucleotides which specifically hybridize to nucleic acids encoding DNA-dependent protein kinase subunits. As detailed above, Housman et. al fail to teach the necessary inhibition of the gene product targeted by applicants' invention. Applicants maintain that Chiorini et al. also fail to teach this element, and therefore, the cited references in combination fail to teach each and every element of the rejected claims.

As the Examiner concedes, Chiorini et al. teach antisense oligonucleotides operatively linked to a heat shock promoter and in an appropriate expression vector. Chiorini et al. does not teach that the antisense oligonucleotide must specifically hybridize to a nucleic acid encoding a DNA-PK subunit *so as to prevent expression of the DNA-PK subunit*.

For the reasons above, the cited references combined fail to teach the elements of the claimed antisense oligonucleotides. Absent such teaching, there could not have been a motive to combine or a reasonable expectation of success.

In view of the above remarks, applicants maintain that the

Examiner has failed to set forth a *prima facie* case of obviousness, and that accordingly, claims 15 and 18-24 satisfy the requirements of 35 U.S.C. §103(a).

Conclusion

For the reasons set forth above, applicants respectfully request that the Examiner reconsider and withdraw the rejections, and solicit allowance of pending claims 1-16 and 18-24.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invite the Examiner to telephone them at the number provided below.

No fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,

I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:
Commissioner for Patents,
P.O. Box 1450
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3/2/07

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